Title: Synthetic Heparin-Binding Factor Analogs

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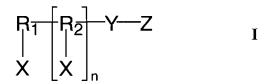
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IN THE CLAIMS

Please replace all prior versions and listings with the following claims listing.

CLAIMS LISTING

1. (withdrawn) A heparin-binding growth factor (HBGF) analog of formula I:



wherein:

each X is a peptide chain that (i) has a minimum of three amino acid residues, (ii) has a maximum of about fifty amino acid residues, and (iii) binds a heparin-binding growth factor receptor (HBGFR);

 R_1 is an amino acid residue, wherein X is covalently bonded through the N-terminus of R_1 or through a side chain of R_1 ;

 R_2 is a trifunctional alpha amino acid residue, wherein X is covalently bonded through a side chain of R_2 ;

Y is a linker comprising a chain from 0 to about 50 atoms covalently bonded to R_1 and Z when n=0, or to R_2 and Z when n=1;

Z is a non-signaling peptide chain that comprises a heparin binding domain, comprising an amino acid sequence that comprises (i) a minimum of one heparin binding motif, (ii) a maximum of about ten heparin binding motifs, and (iii) a maximum of about thirty amino acids; and,

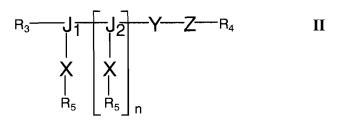
n is 0 or 1, wherein when n=1 the peptide chains X are identical.

2. (withdrawn) The heparin-binding growth factor analog of claim 1 wherein X and Z are synthetic peptide chains.

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3. (withdrawn) The heparin-binding growth factor analog of claim 1 or 2 wherein Y further comprises a linker that (i) is hydrophobic, (ii) comprises a chain of a minimum of about 9 and a maximum of about 50 atoms, and (iii) is not found in the natural ligand of the heparin-binding growth factor receptor (HBGFR) which X binds.

- 4. (withdrawn) The heparin-binding growth factor analog of claim 1 or 2 wherein R_1 is a trifunctional amino acid residue, wherein X is covalently bonded through a side chain of R_1 .
- 5. (withdrawn) The heparin-binding growth factor analog of claim 1 or 2 wherein the heparin-binding growth factor analog has an avidity for heparin such that the synthetic heparin-binding growth factor analog binds heparin in 0.15 M NaCl, but is eluted by 1 M NaCl.
- 6. (withdrawn) The heparin-binding growth factor analog of claim 1 or 2, consisting essentially of a molecule of formula (I).
- 7. (withdrawn) The synthetic heparin-binding growth factor analog of claim 1 or 2, consisting of a molecule of formula (I).
 - 8. (currently amended) A heparin-binding growth factor (HBGF) analog of formula II:



wherein:

 R_3 and R_5 are each independently NH_2 , an acyl group with a linear or branched C_1 to C_{17} alkyl, aryl, heteroaryl, alkene, alkenyl or aralkyl chain including an N-terminus NH_2 ,

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NH₃⁺, NH group or a corresponding acylated derivative, or is an amino acid, a dipeptide or a tripeptide with an N-terminus NH₂, NH₃⁺, NH group or a corresponding acylated derivative;

R₄ is -OH, NH₂, NH-R₆, or is an amino acid, a dipeptide or a tripeptide with a Cterminus -OH, NH₂, or NH-R₆;

 R_6 is an aliphatic C_1 to C_{17} chain;

each X is comprises a peptide chain that (i) has a minimum of three amino acid residues, (ii) has a maximum of about fifty amino acid residues, and (iii) binds a heparin-binding growth factor receptor (HBGFR) is selected from SEQ ID NO: 6-21;

J₁ and J₂ are each independently a trifunctional alpha amino acid residue, wherein each X is covalently bonded through a side chain of J_1 or J_2 ;

Y is a linker comprising a chain from 0.6 atoms to about 50 atoms covalently bonded to J₁ and Z when n=0, or to J₂ and Z when n=1 three amino hexanoic acid residues;

Z is a non-signaling peptide that comprises a heparin binding domain, comprising SEQ ID NO: 2;

(i) a minimum of one heparin binding motif, (ii) a maximum of about ten heparin binding motifs, and (iii) a maximum of about thirty amino acids; and,

n is 0 or 1, wherein when n=1 the synthetic peptide chains X are identical.

9. (original) The heparin-binding growth factor analog of claim 8 wherein X and Z are synthetic peptide chains.

10-11. (canceled)

12. (currently amended) The heparin-binding growth factor analog of claim 8, 9 or 10 wherein the heparin-binding growth factor analog has an avidity for heparin such that the heparin-binding growth factor analog binds heparin in 0.15 M NaCl, but is eluted by 1 M NaCl. AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

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13. (currently amended) The heparin-binding growth factor analog of claim 8, 9 or 10 wherein binding of the heparin-binding growth factor analog to the heparin-binding growth

factor receptor initiates a signal by the heparin-binding growth factor receptor.

14. (currently amended) The heparin-binding growth factor analog of claim 8, 9 or

10 wherein binding of the heparin-binding growth factor analog to the heparin-binding growth

factor receptor blocks signaling by the heparin-binding growth factor receptor.

15. (currently amended) The heparin-binding growth factor analog of claim 8, 9 or

10 wherein J_1 and, if n = 1, J_2 is a diamine amino acid residue.

16. (original) The heparin-binding growth factor analog of claim 15 wherein the diamine

amino acid residue is a 2,3 diamino propionyl amino acid residue.

17. (original) The heparin-binding growth factor analog of claim 15 wherein the diamine

amino acid residue is lysine.

18. (original) The heparin-binding growth factor analog of claim 15 wherein the diamine

amino acid residue is ornithine.

19. (currently amended) The heparin-binding growth factor analog of claim 8, 9 or

10 wherein the covalent bond between X and J_1 or, if n=1, J_2 , comprises a peptide, disulfide,

thioether, Schiff base, reduced Schiff base, imide, secondary amine, carbonyl, urea, hydrazone or

oxime bond.

The heparin-binding growth factor analog of claim 8, 9 or 20. (currently amended)

 $\frac{10}{10}$ wherein the side chain of J_1 and, if n=1, J_2 , comprises a reactive carboxyl group.

21. (withdrawn) The heparin-binding growth factor analog of claim 8, 9 or 10 of

formula III:

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wherein m is from 1 to about 10.

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22. (withdrawn) The heparin-binding growth factor analog of claim 21 of formula IV:

wherein p is from 1 to about 10 and q is from 1 to about 20.

23. (withdrawn) The heparin-binding growth factor analog of claim 22 wherein p is 5, q is three, Z is SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5, and X is SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20 or SEQ ID NO:21.

- 24. (withdrawn) The heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22 wherein the peptide chain X has a minimum of approximately five amino acid residues.
- 25. (withdrawn) The heparin-binding growth factor analog of claim 24 wherein the peptide chain X has a minimum of approximately nine amino acid residues.
- 26. (withdrawn) The heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22 wherein the peptide chain X has a maximum of approximately thirty three amino acid residues.

27-31. (canceled)

32. (currently amended) The heparin-binding growth factor analog of claim 31 8 wherein the heparin-binding growth factor analog binds an FGF receptor.

33. (canceled)

34. (currently amended) The heparin-binding growth factor analog of claim $\frac{1}{2}$, $\frac{2}{3}$,

8, 9, 10, 21 or 22 wherein the heparin-binding growth factor analog is an antagonist of the

heparin-binding growth factor receptor.

35. (currently amended) The heparin-binding growth factor analog of claim $\frac{1}{2}$, $\frac{2}{3}$,

8, 9, 10, 21 or 22 wherein the heparin-binding growth factor analog is a positive modulator of the

biological response to a heparin-binding growth factor.

36. (currently amended) The heparin-binding growth factor analog of claim $\frac{1}{2}$, $\frac{2}{3}$,

8, 9, 10, 21 or 22 wherein the heparin-binding growth factor analog is a negative modulator of

the biological response to a heparin-binding growth factor.

37. (currently amended) The heparin-binding growth factor analog of claim $\frac{1}{2}$, $\frac{2}{3}$,

8, 9, 10, 21 or 22 wherein the peptide chains X are cross-linked or cyclized.

38. (original) The heparin-binding growth factor analog of claim 37 wherein the peptide

chains X are cross-linked or cyclized by at least one disulfide, peptide, or thioether bond.

39-45. (canceled)

46. (withdrawn) A pharmaceutical composition comprising the heparin-binding growth

factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22 or a pharmaceutically acceptable salt thereof and

a pharmaceutical carrier.

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47. (withdrawn) A method for treating a mammal that is exposed to a harmful dose of radiation or a chemotherapeutic agent, the method comprising administering to the mammal an effective dose of a heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22.

- 48. (withdrawn) A method for treating a mammal that is exposed to a harmful dose of radiation or a chemotherapeutic agent, the method comprising administering to the mammal an effective dose of a heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22 wherein X binds an FGF receptor.
- 49. (withdrawn) The method of claim 47or 48 wherein the dose of radiation or chemotherapeutic agent is sufficient to cause mucositis, G.I. syndrome, or radionecrosis.
 - 50. (withdrawn) The method of claim 48 wherein the FGF receptor is an FGF-7 receptor.
- 51. (withdrawn) A method for stimulating growth factor receptor signaling in a cell, the method comprising contacting the cell with an effective amount of a heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22.
- 52. (withdrawn) The method of claim 51 wherein the signaling stimulates proliferation of the cell.
 - 53. (withdrawn) The method of claim 52 wherein the cell is part of a mammal.
- 54. (withdrawn) A method for delivering an active heparin-binding growth factor analog to a mammal, the method comprising:

providing a medical device coated on the surface thereof via non-covalent bonds with a synthetic heparin-binding growth factor analog of claim 1, 2, 3, 8, 9, 10, 21 or 22; and

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placing the medical device onto a surface of, or implanting the medical device into, the mammal.

55. (withdrawn) The method of claim 54 wherein the medical device is a suture, graft material, wound covering, nerve guide, bone wax, aneurysm coil, embolization particle, microbead, stint, dental implant, or bone prosthesis, a tissue scaffold or a controlled release drug delivery device.

56. (withdrawn) The method of claim 54 wherein the non-covalent bonds are associations between the heparin-binding domain of the synthetic heparin-binding growth factor analog and a heparin-containing compound bound to the surface of the medical device.

- 57. (withdrawn) The method of claim 56 wherein the heparin-containing compound is benzyl-bis(dimethylsilylmethyl)oxycarbamoyl-heparin.
- 58. (withdrawn) The method of claim 54 wherein the surface of the medical device is stainless steel, titanium, platinum, tungsten, ceramics, polyurethane, polytetrafluoroethylene, extended polytetrafluoroethylene, polycarbonate, polyester, polypropylene, polyethylene, polystyrene, polyvinyl chloride, polyamide, polyacrylate, polyurethane, polyvinyl alcohol, polycaprolactone, polyactide, polyglycolide, polysiloxanes, natural rubbers, artificial rubbers, block polymers, or copolymers of block polymers.
- 59. (withdrawn) The method of claim 58 wherein the polysiloxane is 2,4,6,8tetramethylcyclotetrasiloxane.